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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/586,374

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EXAMINER

SWOPE, SHERIDAN

ART UNIT

PAPER NUMBER

1652

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/586,374	Applicant(s) DONALD ET AL.	
	Examiner SHERIDAN SWOPE	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-19 and 38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-19 and 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicants' filing of May 21, 2009, in response to the action of March 13, 2009, is acknowledged. It is acknowledged that Claims 12, 13, 15- 17, 19 and 38 are amended. Claims 12-19 and 38 are pending and are hereby reexamined.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-19 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

Rejection of Claim 12, lines 7-8, because "an amino acid sequence of SEQ ID NO: 2" renders the claim indefinite is maintained. Rejection of Claims 13-15 and 38, as dependent from Claim 12, is maintained for the same reason.

Rejection of Claim 38, because the phrase "encodes the amino acid sequence as set forth by SEQ ID NO: 2" renders the claim indefinite, for the reasons explained in the prior action, is maintained.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claim 12, and dependent Claims 13-15, under 35 U.S.C. 112, first paragraph, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) Claim 12 has been amended to encompass nucleotide sequences that encode the protein of SEQ ID NO: 2 (part (a)), nucleotide sequences that hybridize either under high stringency conditions to the complement of a nucleic acid molecule encoding SEQ ID NO:2 (part (b)) or under moderate stringency conditions to the complement of SEQ ID NO: 1 (part (c)), wherein the nucleotide sequence encodes an amino acid sequence 80% identical to SEQ ID NO: 2. This is contrary to the Office Action's finding that claim 12 encompasses "any CKI protein having at least 80% identity to SEQ ID NO: 2."

(B) The specification discloses sequences for three novel coccidian CKI proteins and compares the sequence structural features of the three novel coccidian CKI proteins to that of other CKI proteins from protozoan parasites (Fig 4; PfCkIGt, LmCkI-2, TcCKI-2). In Figure 4, the brackets delineate the boundaries of the catalytic core region of the enzymes, representing the region of greatest homology.

(C) CKI assays are described.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: It is acknowledged that Claim 12 has been amended. Claim 12(c) recites a nucleic acid molecule that hybridizes to the complement of SEQ ID NO: 1 under conditions of 0.2X SSC/1% SDS at 42°C, wherein the nucleic acid molecule encodes a protein having at least 80% identity to SEQ ID NO: 2. The skilled artisan would know that the genus of all nucleic

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acid molecule that hybridizes to the complement of SEQ ID NO: 1 under conditions of 0.2X SSC/1% SDS at 42°C is, more likely than not, the same or larger than the genus of all nucleic acid molecule that encode a protein having at least 80% identity to SEQ ID NO: 2. The cloning all said polynucleotides, identification of all encoded proteins having at least 80% identity to SEQ ID NO: 2, and testing all said proteins for the desired activity represents undue experimentation.

The number of variants increases exponentially as the percent identity decreases. The genus of any protein having at least 80% homology to a parent protein of 335 residues (SEQ ID NO: 2) can be described by $(19_1 + 19_2 + 19_3 + \dots 19_{335})^{20} = 1.2 \times 10^{76}$ variants. Even if the hybridization limitation in step (c) eliminated 90% of said variants the number of variants to be analyzed at the protein level is still 1.2×10^{75} . Guo et al, 2004 teaches that the percentage of random single-substitution mutations, which inactivate a protein, using a protein 3-methyladenine DNA glycosylase as a model, is 34% and that this number is consistent with other studies in other proteins (pg 9206, parag 4). Guo et al further shows that the percentage of active mutants for multiple mutations appears to be exponentially related to this by the simple formula $(.66)^x \times 100\%$ where x is the number of mutations introduced (Table 1). Applying this estimate to the protein recited in the instant application, 80% identity allows up to 67 mutations within the 335 amino acids of SEQ ID NO:2 and, thus, only $(.66)^{67} \times 100\%$ or $8.1 \times 10^{-11}\%$ of random mutants having 80% identity would be active. Current techniques in the art (i.e., high throughput mutagenesis and screening techniques) would allow for finding a few active mutants within several hundred thousand or up to about a million inactive mutants, despite even this being an enormous quantity of experimentation that would take a very long time to accomplish. But

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finding a few mutants within several billion or more, as in the claims to at least 80% identity herein, would not be possible. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Sufficient guidance has **not** been provided in the instant specification.

(B) Reply: Regarding the information in Figure 4, the following comments are made. Of the three “CKI proteins” from protozoan parasites neither LmCKI/ GenBank Accession No. AAF35365 nor TcCKI-2/ GenBank Accession No. AAF00025 have been shown to have CKI activity. Thus, alignment of said parasitic proteins with SEQ ID NO: 2 provides no guidance on structural requirements for CKI activity. In additions, the assertion that residues 4-275 of SEQ ID NO: 2 represents the catalytic domain provides no substantial guidance as to which residues of this 335 amino acid protein may, or may not, be altered and still retain the desired activity.

It is acknowledged that the specification discloses, in addition to SEQ ID NO: 2, two other CKI proteins having 48% and 81% identity with SEQ ID NO: 2, while the parasitic PfCKI.alpha CKI/GenBank Accession No. AF017139 has 67% identity with SEQ ID NO: 2. The alignment of said three proteins with SEQ ID NO: 2 provides some, very limited guidance as to which residues and motifs may, or may not, be altered and still retain the desired activity. However, in the absence of structure/functions studies, such as mutational analysis and crystallography, this limited guidance is not sufficient such that the skilled artisan can make and use the full scope of the recited invention without undue experimentation. See (A), above.

(C) Reply: It is acknowledged that CKI assays were known in the art.

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For these reasons and those explained in the prior action, rejection of Claim 12, and dependent Claims 13-15, under 35 U.S.C. 112, first paragraph, is maintained.

Allowable Subject Matter

No claims are allowable.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Any new references were cited solely to support rejection(s) based on amendment or rebut Applicants' arguments. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants'

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remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that the serial number of the application and date of amendment be referenced on every page of the response.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652